SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

EXCLUDER™ Bifurcated Endoprosthesis (EBE)

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Summary of Safety and Effectiveness Data (SSED)

EXCLUDER™ Bifurcated Endoprosthesis

1.0 General Information

Device Generic Name……………….Endovascular Graft

Device Trade Name………………….EXCLUDER Bifurcated Endoprosthesis

Applicant's Name and Address……..W. L. Gore and Associates, Inc.
1327 Orleans Drive
Sunnyvale, CA 94089

PMA Application Number……….. …..M000014/PMA

2.0 Indications and Usage

The EXCLUDER Endoprosthesis is intended to exclude the aneurysm from the blood circulation in patients diagnosed with infrarenal AAA disease and who have appropriate anatomy.

3.0 Contraindications

Known contraindications include, but are not limited to:

- significant thrombus at the arterial implantation sites, specifically proximal aortic neck and distal iliac artery interface
- severe proximal aortic neck angulation >60º
- infrarenal aortic neck <15 mm in length
- illio-femoral access vessel morphology which is not compatible with vascular access techniques, devices and accessories.

4.0 Warnings and Precautions

See Warnings and Precaution in the labeling (Instructions for Use)

5.0 Device Description

The EXCLUDER Bifurcated Endoprosthesis is comprised of an implantable prosthesis (endoprosthesis) and a catheter delivery system. The EXCLUDER Bifurcated Endoprosthesis System consists of four modular components (Figures 5-1 to 5-4). The two primary modular components are the Trunk-Ipsilateral Leg and the Contralateral Leg. There are also two optional components, the Aortic Extender and Iliac Extender. Each component is loaded onto its own delivery catheter and is packaged separately.

The Trunk-Ipsilateral Leg component is a single aorta-sized ultra-thin expanded polytetrafluoroethylene (ePTFE) tube, with an external nitinol supporting structure which bifurcates into two smaller tubes (Figure 5-1). One tube forms the longer Ipsilateral Leg limb, and the other a shorter Contralateral Leg Hole. A radiopaque ring of gold wire is embedded in the Contralateral Leg Hole for visualization of the leg hole after deployment. The external nitinol supporting structure consists of a nitinol wire shaped into an undulating helix. The nitinol supporting structure is located on the outside of the graft material, and is attached to the graft material with tape made of ePTFE and fluorinated ethylene propylene (FEP). On the proximal end of the device, nitinol anchors are incorporated into the supporting stent structure, and angle away from the stent to provide anchoring support against the vessel. The proximal end of the device also contains an external sealing cuff to aid in preventing blood flow around the outside of the device.

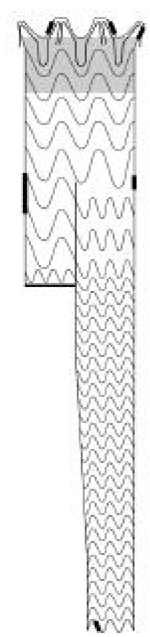

Figure 5-1. Trunk-Ipsilateral Leg Endoprosthesis

The Contralateral Leg is a separate component which is placed in the Trunk-Ipsilateral Leg. The Contralateral Leg consists of a tapered expanded polytetrafluoroethylene (ePTFE) tube, an external nitinol supporting stent structure, and radiopaque markers which aid in proper positioning (Figure 5-2).

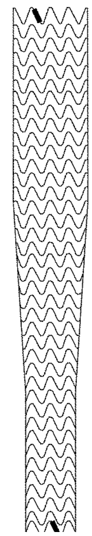

Figure 5-2. Contralateral Leg Endoprosthesis

The Aortic Extender (Figure 5-3) is intended to be used electively after the EXCLUDER Bifurcated Endoprosthesis is placed in the abdominal aorta. The Aortic Extender is intended to be used when additional length and/or sealing for aneurysmal exclusion are desired. The Aortic Extender is placed inside of the EXCLUDER Bifurcated Endoprosthesis. It is a straight ePTFE tube with a nitinol supporting stent structure, and radiopaque markers. It is compressed to a small diameter inside a sleeve and mounted onto a delivery catheter.

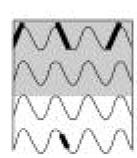

Figure 5-3. Aortic Extender Endoprosthesis

The Iliac Extender (Figure 5-4) is intended to be used electively after deployment of the EXCLUDER Bifurcated Endoprosthesis. The Iliac Extender provides additional overall device length flexibility and/or sealing for aneurysmal exclusion. The endoprosthesis can be inserted into either the Contralateral or Ipsilateral leg component of the EXCLUDER Bifurcated Endoprosthesis. The Iliac Extender consists of a tapered expanded polytetrafluoroethylene (ePTFE) tube, an external nitinol supporting stent structure, and radiopaque markers.

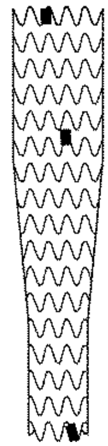

Figure 5-4. Iliac Extender Endoprosthesis

The EXCLUDER Endoprostheses are constrained with an ePTFE sleeve and are packaged separately on the leading end of the delivery catheter (Figure 5-5). The delivery catheters for the Trunk-Ipsilateral Leg, Contralateral Leg, Aortic and Iliac Extender Delivery Systems are similar in materials and operation. All the catheters consist of stainless steel braid-reinforced outer shaft tubing, two olives (oval beads) on either side of the constrained endoprosthesis, a proximal adapter, a single lumen inner tubing for the guidewire and a separate lumen for the deployment line. An ePTFE deployment line, used to sew the sleeve closed, is located within the deployment lumen of the catheter shaft. The deployment line then leads to the deployment knob within the proximal adapter. Thus the deployment line, the deployment knob and the sleeve represent the deployment system.

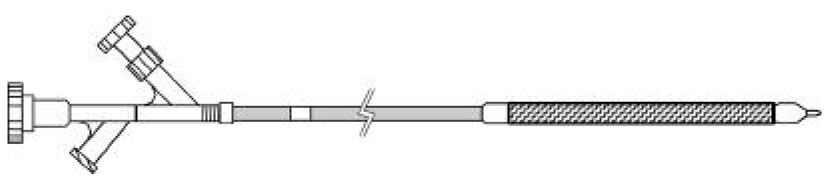

Figure 5-5. EXCLUDER Endoprosthesis Delivery Catheter

All the endoprostheses are available in a range of lengths and diameters to accommodate variations in patient anatomy. The following tables (5.1-5.4) list the Part Number and sizes for the Bifurcated EXCLUDER Endoprosthesis (Trunk-Ipsilateral Leg and the Contralateral Leg) and the EXLUDER Extender Endoprosthesis (Aortic and Iliac).

Table 5.1. Trunk-Ipsilateral Leg Sizes

Part Number	Endoprosthesis Aortic Diameter [mm]	Endoprosthesis Iliac Diameter [mm]	Endoprosthesis Length [cm]
PCT231216	23	12	16
PCT231218	23	12	18
PCT231416	23	14.5	16
PCT231418	23	14.5	18
PCT261216	26	12	16
PCT261218	26	12	18
PCT261416	26	14.5	16
PCT261418	26	14.5	18
PCT281216	28.5	12	16
PCT281218	28.5	12	18
PCT281416	28.5	14.5	16
PCT281418	28.5	14.5	18

Table 5.2. Contralateral Leg Endoprosthesis Sizes

Part Numbers	Endoprosthesis Proximal Diameter [mm]	Endoprosthesis Iliac Diameter [mm]	Endoprosthesis Length [cm]
PCC121000	16	12	10
PCC121200	16	12	12
PCC121400	16	12	14
PCC141000	16	14.5	10
PCC141200	16	14.5	12
PCC141400	16	14.5	14

Table 5.3. Aortic Extender Endoprosthesis Sizes

Part Numbers	Endoprosthesis Diameter [mm]	Endoprosthesis Lengths [cm]
PCA230300	23	3.3
PCA260300	26	3.3
PCA280300	28.5	3.3

Table 5.4. Iliac Extender Endoprosthesis Sizes

Part Numbers	Endoprosthesis Proximal Diamete [mm]	Endoprosthesis Iliac Diameter [mm]	Endoprosthesis Length [cm]
PCL161007	16	10	7
PCL161207	16	12	7
PCL161407	16	14.5	7

6.0 Alternative Practices and Procedures

The generally accepted treatment for AAA repairs is surgical repair, which involves dissecting the aneurysm and placing a synthetic graft inside the diseased tissue. AAA diagnosed patients who are considered good or acceptable surgical and anesthetic risk are recommended for elective surgical repair when the aneurysm shows rapid growth, becomes symptomatic, or reaches a maximum diameter generally greater than 4.5 cm.

AAA diagnosed patients who are considered unacceptable surgical or anesthesia risk candidates may be medically managed and closely monitored, recommended for endovascular repair, or elect to forego treatment and eventually succumb to death due to rupture or comorbid disease.

7.0 Marketing History

The EXCLUDER Bifurcated Endoprosthesis has been commercially available in many countries throughout the world, including Europe, Asia, Latin America and Australia. The EXCLUDER Bifurcated Endoprosthesis has not been withdrawn from marketing in any country for any reason, including safety or effectiveness.

8.0 Adverse Events

Table 8.1. Major Adverse Events according to Type, Time and Study Group

Major Adverse Events	Early (≤ 30 days)				Late (> 30 days to 12-months)			
	EBE		Control		EBE		Control	
	%	235	%	99	%	231	%	97
Deaths	1	3	0	0	6	14	5	5
Other Adverse Events								
Bleeding	4	10	32	32	0.4	1	1	1
Pulmonary	1	3	12	12	4	10	4	4
Cardiac	3	7	14	14	7	16	13	13
Renal	1	2	3	3	2	5	0	0
Wound	3	7	4	4	4	9	2	2
Bowel	2	5	16	16	3	6	3	3
Vascular	1	3	6	6	3	7	5	5
Endoleak with an Intervention	0	0	NA	NA	6	13	NA	NA
Aneurysm size increase with an Intervention	0	0	NA	NA	0.4	1	NA	NA
Neurologic	0.4	1	2	2	3	7	1	1
Genitourinary	0.4	1	1	1	3	6	1	1
Neoplasm	0.4	1	0	0	1	3	1	1
Other Complications	0	0	2	2	5	12	4	4

9.0 Summary of Pre-clinical Results

9.1 Biocompatibility

Toxicology and biocompatibility testing was conducted for materials in the EXCLUDER Bifurcated Endoprosthesis System. Testing was conducted in accordance with Federal Good Laboratory Practices per 21 CFR §58. The EXCLUDER Bifurcated Endoprosthesis was classified per ISO 10993 as an implant device with permanent contact. The EXCLUDER delivery catheter was classified as an externally communicating device with limited exposure (? 24 hr).

The EXCLUDER Bifurcated Endoprosthesis is made of gold radiopaque markers, ePTFE (expanded polytetrafluoroethylene), ePTFE/FEP (fluorinated tape) and nickel titanium alloy (nitinol). Historically, ePTFE and FEP have been characterized as safe biomaterials. Literature reviews have documented that ePTFE and FEP have an acceptable long term history of human implantation.

The materials used to manufacture the delivery catheters are commonly used in other commercially available medical devices, such as percutaneous transluminal coronary angioplasty (PTCA) catheters, peripheral transluminal angioplasty (PTA) catheters, and ePTFE sutures. The materials in these devices have been documented and have been demonstrated to be safe to use in limited-duration, blood-contacting medical devices. No component of the catheter is intended to have greater than limited (? 24 hr) contact with the patient.

Table 9.1 summaries the biocompatibility test results for the implant. Table 9.2 summarizes the biocompatibility test results for the catheter.

Table 9.1. Summary of Biocompatibility Test Results for the Implant

Test Name	Test Method	Results
Cytotoxicity	MEM Elution Test – ISO	Non-Cytotoxic
Sensitization	Kligman Maximization Study – ISO	Non-Sensitizing
Irritation/Intracutaneous Toxicity	Intracutaneous Injection Test - ISO	Negligible Irritant
Acute Systemic Toxicity	Systemic Injection Test - ISO	No significantly greater biological reaction than the controls.
Pyrogenicity	Rabbit Pyrogen Test (Material Mediated) -ISO	Non-Pyrogenic
Hemocompatibility	Hemolysis: Direct Contact-Rabbit Blood – ISO	Non-Hemolytic
Subchronic Toxicity	Canine Implant Study	No Systemic Effects Observed
Genotoxicity/Mutagenicity	*Salmonella typhimurium* and *Escherichia coli* Reverse Mutation Assay –ISO	Non-Mutagenic
	CHO/HGPRT Forward Mutation Assay –ISO	Non-Mutagenic
	Chromosomal Aberration Assay –ISO	Non-Clastogenic
Implantation	Intramuscular Implantation –ISO	Test Article and Negative Control had Comparative Results
Chronic Toxicity	Canine Implant Study	No Systemic Effects Observed

Table 9.2. Summary of Biocompatibility Test Results for the Catheter

Test Name	Test Method	Results
Cytotoxicity	MEM Elution Test – ISO	Non-Cytotoxic
Sensitization	Kligman Maximization Study – ISO	Non-Sensitizing
Irritation/Intracutaneous Toxicity	Intracutaneous Injection – ISO	Negligible Irritant
Acute Systemic Toxicity	Systemic Injection Test – ISO	Non-Toxic
Pyrogenicity Test	Rabbit Pyrogen Test (Material Mediated) – ISO	Non-Pyrogenic
Hemocompatibility	Hemolysis Rabbit Blood – ISO	Non-Hemolytic

All test results indicate that the materials and processes used to manufacture the EXCLUDER implant and catheter are biocompatible and suitable for their intended use.

9.2 Animal Studies

Three preclinical *in vivo* studies were conducted to evaluate the performance of the EXCLUDER Bifurcated Endoprosthesis. A canine model was used to assess the ability of the delivery system to successfully access the target site, deploy the graft and be withdrawn from the vasculature, to assess device functionality, and to assess the sub-chronic and chronic biological response to the implanted endoprosthesis. A bovine model was used for acute assessment, in a near human-size animal model, of the delivery system to successfully access the target site, deploy the graft and be withdrawn from the vasculature, and the ability of the device to resist migration. A summary of these studies follows in Table 9.3.

Table 9.3. Summary of Preclinical *In Vivo* Studies

Animal Study	#/ Type of Animal	Test Article	Methods	Results/ Conclusions
Sub-chronic and Chronic Study of Bifurcated Endoprosthesis	15 Canines	Scaled-down, trunk-ipsilateral leg, contralateral leg devices, and delivery catheter.	Catheter delivery and device functionality were assessed sub-chronically and chronically in 15 animals. Two sub-chronic animals were maintained in life for approximately one week. Additionally, three canines were maintained in life for one month, one canine for two months, three canines for three months, and four canines for six months. Two canines in the chronic phase were retrieved within one day post-op.	All devices were successfully delivered and deployed. The functional requirements of the device were met and the devices performed as intended. All devices were patent at retrieval, and the host tissue response was judged to be acceptable at both gross and histological examination. There was no evidence of device/component migration or graft disruption.
Acute Study of Bifurcated Endoprosthesis	6 Bovines	Human size, trunk-ipsilateral leg, contralateral leg devices, and delivery catheter.	Six bovines were assessed for acute delivery catheter and device functionality.	All devices were successfully and accurately deployed. The devices were patent and exhibited normal antegrade flow after deployment. There was no evidence of migration or graft disruption.
Acute Study of Aortic and Iliac Extenders	2 Bovines	Human size, aortic and iliac extender devices. Short trunk endoprosthesis and delivery catheter.	Six aortic extenders on long catheters, six iliac extenders on catheters, and six short trunks were deployed in two bovines. These animal procedures were assessed for acute delivery catheter and device performance of the aortic and iliac extender components.	All devices were successfully deployed. Both aortic and iliac extenders could be accurately placed and deployed within another stent-graft or separately. Radiographic evidence showed that no migration had occurred during the acute phase. Post-deployment angiography showed patency.

9.3 Product Testing

W.L. Gore and Associates, Inc. (GORE), conducted comprehensive pre-clinical bench and analytical testing on the EXCLUDER Bifurcated Endoprosthesis (EBE) implant and delivery system. The express intent of this *in vitro* testing was to verify that the performance attributes of the EBE system are sufficient to minimize the risk of adverse events under anticipated clinical use conditions. Results obtained from the *in vitro* test regimen provide evidence substantiating the safety and effectiveness of the EBE system.

A summary of results is presented below for each of the *in vitro* tests. Table 9.4 summarizes test results associated with the functional requirements of the delivery system, and Table 9.5 summarizes test results related functional requirements of the implant.

The results of the *in vitro* testing, taken as a whole, demonstrate that the EBE system meets established functional requirements for aortic endovascular devices. Furthermore, these data substantiate the safety and effectiveness of the EBE system, which, consequently, is expected to perform as intended when used in accordance with its labeled indications.

9.3.1 Delivery System Test Results Summary

The following table contains test results that were performed to evaluate the ability of the EBE delivery system to access the implant location, accurately deploy the device, safely withdraw the delivery system catheter, maintain hemostasis, and be fluoroscopically visualized.

Table 9.4. Summary of Test Results Related to the EBE Delivery System Functionality

In Vitro Test	Relevant Functional Requirement	Summary of Test Results
Catheter Angular Rotation to Failure Test	?? Ability to access the intended location ?? Ability to deploy the implant ?? Ability to withdraw the delivery system	Finished delivery catheters were tested to determine angular rotation to failure. All delivery systems tested for angular rotation to failure conformed to established design specifications. Based on the results of these tests, the EBE delivery catheters would not be expected to fail in torsion during anticipated clinical use.
Catheter Bond Tensile Strength Test	?? Ability to access the intended location ?? Ability to deploy the implant ?? Ability to withdraw the delivery system	The longitudinal tensile strength of the critical bonds and joints of the EBE delivery catheters were determined. Results indicate that there is at least 95% confidence level that the minimum tensile strength of each critical catheter junction will exceed the ISO 10555-1 standard of 3.37lbf.
Catheter Deployment Knob-Line Assembly Tensile Test	?? Ability to deploy the implant	The tensile strength of the catheter deployment knob/line assembly was determined to demonstrate conformance to design requirements. The data demonstrates that there is at least 95% confidence that there is a 95% probability that any individual deployment knob/line tensile strength exceeds the maximum expected deployment force.
Catheter Leak Test	?? Hemostasis of the delivery system	The leak resistance of the delivery catheters was evaluated. No catheter leakage was observed in any of the test samples when tested up to pressures of 20 atmospheres. These data indicate there is a 95% confidence that there is at least a 95% probability that any EBE delivery catheter will meet the minimum design requirement of 1.5 atm.
Catheter Length Test	?? Ability to access the intended location ?? Ability to deploy the implant	The minimum and maximum expected catheter working lengths for all tested delivery system configurations met the established design specifications at a minimum confidence level of 95%.
Catheter Profile Test	?? Ability to access the intended location ?? Ability to deploy the implant ?? Ability to withdraw the delivery system ?? Hemostasis of the delivery system	All tested catheters met the design specifications with at least 95% confidence. Compatibility with recommended introducer sheath accessories is expected.
Catheter Torsional Bond Strength Test	?? Ability to access the intended location ?? Ability to deploy the implant ?? Ability to withdraw the delivery system	The torsional strength of the two catheter junctions that will be subjected to the greatest torsional load during deployment were determined to have torsional bond strengths significantly in excess of established design specifications.

In Vitro Test	Relevant Functional Requirement	Summary of Test Results
Delivery System Accessory Compatibility	?? Ability to access the intended location ?? Ability to deploy the implant ?? Ability to withdraw the delivery system ?? Hemostasis of the delivery system	All delivery system configurations were dimensionally compatible with the recommended guidewires and introducer sheaths per established design specifications.
Delivery System Deployment Force Test	?? Ability to deploy the implant	The force required to deploy the EBE was determined. The maximum expected deployment force does not exceed the minimum expected strength of the EBE delivery catheter deployment knob/line tensile strength.
Delivery System Deployment Reliability Test	?? Ability to access the intended location ?? Ability to deploy the implant ?? Ability to withdraw the delivery system	A comprehensive evaluation of *in vitro* deployments was conducted. Binomial statistics demonstrate with a 95% confidence level that at least 98% of the EBE will access the intended implant location, safety deploy the implant, and be successfully withdrawn when used in a manner consistent with labeling or under anticipated clinical use.
Delivery System Radiopacity Confirmation Test	?? Fluoroscopic visualization	The results of the *in vitro* radiopacity testing show that the radiopacity of the EBE delivery systems have sufficient radiopacity for clinical use.
Delivery System Torquability Test	?? Ability to access the intended location ?? Ability to deploy the implant ?? Ability to withdraw the delivery system	The torque response of the delivery system and the torque effect on deployment reliability were evaluated. All tested delivery systems exhibited acceptable torque response after being tracked through an *in vitro* aneurysmal deployment model. All tested delivery systems deployed successfully after being subjected to design-specific torque testing.
Sewn Sleeve (Corset) Burst Strength Test	?? Ability to access the intended location ?? Ability to deploy the implant	The burst strength of representative corsets was characterized and determined to be adequate to constrain the stent-graft prior to implantation.

9.3.2 Implant Test Results Summary

The following table contains tests results that were performed to assess the EBE implant's ability to accurately deploy, fixation effectiveness, durability, ability to exclude the aneurysm (permeability considerations), modularity, sizing, patency, and MRI compatibility, and ability to be fluoroscopically visualized.

Table 9.5. Summary of Test Results Related to the EBE Implant Functionality

***In Vitro* Test**	**Relevant Functional Requirement**	**Summary of Test Result**
Acute Anchoring Test	?? Fixation effectiveness of the implant	Acute resistance to migration of the EBE was demonstrated under simulated physiological conditions when used in a manner consistent with those set forth in the Instructions for Use (over-sizing, appropriate device placement, post-deployment balloon touch-up).
Accelerated Anchor Fatigue Test	?? Durability and integrity of the implanted device	Anchor fatigue resistance was evaluated for 10 years simulated physiological loading (380 million cycles) under “worst-case” test conditions. Samples were subjected to severe loading, far in excess of clinically expected loads. Only one anchor fatigue fracture out of 112 tested anchors was noted at the ten-year equivalent inspection. The fractured anchor was attached to the stent-graft. No compromise of device function was noted. From the data generated from this “worst-case” testing, it is expected that the anchors will survive ten years of pulsatile loading under anticipated physiological conditions without fatigue related anchor fracture or compromise of device fixation.
Deployment Accuracy Test	?? Ability to accurately deploy	The Aortic Extender was selected for deployment testing as it is the component most likely to produce deployment inaccuracies. Based on testing in straight and angulated segments of an *in vitro* test model, the EBE is expected to be deployed no more than 5 mm proximal to the intended implant site at a 95% confidence level.
Endoprosthesis Radiopacity Confirmation Test	?? Fluoroscopic visualization	The radiographic visibility of the EBE was determined to be sufficient for clinical use when compared to clinically validated devices under a range of simulated tissue densifications.
Finite Element Analysis	?? Durability and integrity of the implanted device	The location and magnitude of the maximum strains in the EBE Nitinol wire frame were analytically determined as a function of radial compression when subjected to catheter loading and an *in vivo* pulsatile loading environment. Peak strain magnitudes at simulated catheter loading are predicted to be below the ultimate tensile strain of the Nitinol wire. Maximum strain locations and values determined from the simulated *in vivo* pulsatile loading were subsequently used as a reference in appropriate *in vitro* testing including pulsatile fatigue testing and wear and migration testing.

In Vitro Test	Relevant Functional Requirement	Summary of Test Result
Integral Water Permeability	?? Fixation effectiveness of the implant ?? Permeability considerations ?? Testing of the modularity of the endovascular system	The integral water permeability of the EBE modular components was determined. Integral Water Permeability of all EBE components was calculated and shown to be between 0.05 and 1.57 ml/min/cm^2. The integral water permeability observed in EBE is less than the water permeability of polyester materials used in endovascular and vascular applications.
Longitudinal Tensile Strength Test	?? Durability and integrity of the implanted device	The longitudinal tensile strength of the EBE components was characterized and compared to the appropriate ePTFE graft design specifications. All tensile strengths exceed the established specifications.
Magnetic Resonance Imaging Safety Test	?? MRI compatibility	The EBE is not expected to present an additional hazard or risk when implanted in a patient subjected to MRI at 1.5-Tesla. There were no observable magnetic field interactions, minimal MRI-related heating (<1.0°C), and only minor image artifacts. The device has therefore been determined to be MRI safe under these conditions.
Microscopic Determination of Porosity Test	?? Permeability considerations ?? Patency of the implant	The fibril length of the ePTFE material comprising the luminal surface of the EBE was determined. The data indicate that the fibril length of the EBE luminal surface is consistent with that of GORE-TEX™ Vascular Grafts successfully used in aortic applications.
Nitinol Material Analysis Test	?? Durability and integrity of the implanted device	The bulk material and surface of the Nitinol wire used for the EBE was chemically analyzed and quantified. The surfaces of the wire were also examined under SEM to detect defects and contamination. The bulk material analysis and surface analysis met design requirements. Surface observations with SEM demonstrated a consistently smooth wire surface with no unacceptable anomalies such as pitting, cracks, or contaminants.
Nitinol Stent Corrosion Resistance Test	?? Durability and integrity of the implanted device	The corrosion resistance of both the Nitinol wire and the complete EBE was analyzed using potentiodynamic polarization testing. The finished EBE device has an average predicted corrosion rate less than 316L stainless steel under the test conditions.

In Vitro Test	Relevant Functional Requirement	Summary of Test Result
Nitinol Thermo-mechanical Properties Test	?? Durability and integrity of the implanted device.	The thermodynamic and mechanical attributes of the Nitinol wire used in the EBE were assessed for conformance with established design specifications. All test articles had an austenitic finish temperatures (AF) below 35°C, and therefore met the established design specifications. Tensile testing was performed on all wire sizes to characterize the mechanical properties of the material. These properties include tensile strength, mean elongation at break, ultimate tensile loading plateau, and tensile permanent set after deformation. The results demonstrate that the mechanical properties of the processed wire meet or exceed, as appropriate, the established acceptance criteria.
Pull Test for Modular Components	?? Testing of the modularity of the endovascular system	The force required to separate the modular components of the EBE in an *in vitro* setting was determined. The average longitudinal separation (pull-out) forces are expected to be sufficient for clinical use.
Pulsatile Fatigue Test	?? Durability and integrity of the implanted device	After 10 years simulated physiological loading of 380 million cycles, tested samples were examined visually and with magnification. There was no evidence of Nitinol wire pitting or cracking, nor of fatigue related fractures. No wear, abrasion, or migration between the overlapping portion of the trunk-ipsilateral leg and contralateral leg were noted. The device was intact after 10 years simulated *in vivo* physiological loading of 380 million cycles with no perforation or detachment of the ePTFE graft as a result of pulsatile fatigue testing.
Radial Compression Strength Test	?? Fixation effectiveness of the implant ?? Appropriate Sizing of the implant ?? Patency of the implant	The radial compression forces of the EBE components were characterized at the appropriate diameters representative of clinically relevant oversizing. The radial compression strengths of the EBE are anticipated to be adequate for clinical use.
Sealing Test	?? Fixation effectiveness of the implant ?? Permeability considerations ?? Testing of the modularity of the endovascular system	The overall rate of fluid loss around and through the various modular components of the EBE when deployed in a flow model was characterized. The total rate of fluid loss for the worst case EBE configurations, inclusive of the leakage at the modular junctions and the permeability of the graft material, approximate the permeability alone of commercially available polyester materials used in vascular and endovascular applications.

In Vitro Test	Relevant Functional Requirement	Summary of Test Result
Stent-Graft Bend Radius Test	?? Ability to accurately deploy ?? Fixation effectiveness of the implant ?? Patency of the implant	The bend radii of the various components of EBE were characterized. Comparison to published literature shows that the EBE System is capable of accommodating typical aorto-iliac anatomy without kinking.
Stent-Graft Burst Strength Test	?? Durability and integrity of the implanted device	The burst strength of the EBE components was determined and compared to the appropriate ePTFE graft design specifications. All burst strengths exceeded the minimum design requirements.
Stent-Graft Diameter and Wall Thickness Test	?? Testing of the modularity of the endovascular system ?? Appropriate sizing of the implant	The outer diameters and wall thickness of the deployed EBE components were characterized and verified. All components tested met the appropriate design requirements.
Stent-Graft Length Test	?? Ability to accurately deploy ?? Appropriate sizing of the implant	The length of the EBE components, mounted on the delivery catheters was measured and compared to relevant design specifications.
Stent-Graft Profile Test	?? Appropriate sizing of the implant	The profiles of the EBE mounted on delivery catheters were assessed to assure dimensional compatibility with recommended introducer sheath sizes.
Wear and Migration Test	?? Fixation effectiveness of the implant ?? Durability and integrity of the implant ?? Testing of the modularity of the endovascular system	Endoprosthesis integrity was intact after 5 and 10 years simulated physiological loading of 190 million and 380 million cycles, respectively. Although test specimens showed artifactual evidence of extensive pulsatile testing, no modular component migration or wire fatigue fracture was noted. Neither significant detachment of the stent-graft, nor any wear-induced perforations were noted. There was no obstruction of the graft lumen.

A robust test and analysis regimen was constructed to characterize the mechanical attributes of the EBE. The results of the *in vitro* testing, taken as a whole, demonstrate that the EBE system meets established functional requirements for aortic endovascular devices. Furthermore, these data substantiate the safety and effectiveness of the EBE system by providing evidence that the mechanical attributes of the device have met design goals appropriate for the repair of abdominal aortic aneurysms.

9.4 Additional Studies

This device contains no software or electrical components.

10.0 Summary of Clinical Studies

10.1 Objectives

The primary objective of the clinical study was to demonstrate that the EXCLUDER Bifurcated Endoprosthesis is a safe and effective alternative to open surgical repair in the primary treatment of infrarenal abdominal aortic aneurysms. Safety was determined by demonstrating that the EXCLUDER Bifurcated Endoprosthesis subjects would have a total proportion of major adverse events that is less that the subjects treated with open repair as evaluated through one year follow-up. Effectiveness was based on exclusion of the aneurysm including the absence of an endoleak, the absence of aneurysm enlargement (≥ 5 mm), and the absence of major device efficacy adverse events evaluated through one year follow-up. Secondary objectives included an assessment of clinical benefit and quality-of-life measures.

10.2 Study Design

This prospective, non-randomized, multi-center clinical study was designed to compare patients treated with endovascular repair to an open surgical repair control group. The control group included patients whose vascular anatomy (proximal aortic neck length, proximal neck angulation, and arterial implantation site condition) may not have been suitable for endovascular AAA repair. The planned ratio of EXCLUDER Bifurcated Endoprosthesis to control patients was 2:1. Follow-up evaluations were scheduled for pre-discharge, 1-month, 3-months (if endoleak at 1-month), 6-months, 12-months and annually thereafter. An independent Core Lab facility reviewed CT scans and abdominal x-rays to assess aneurysm diameter changes, device and relative component migration, device integrity (wire and graft) and the presence and type of endoleaks.

10.3 Description of Subjects

Nineteen U.S. sites enrolled 235 EXCLUDER Bifurcated Endoprosthesis and 99 control subjects. Given the epidemiology of AAA and surgical repair, males predominated over females (83% compared to 17%). The selection criteria for the study were based on enrolling subjects with the appropriate anatomy for endovascular repair. A total of 31 females were treated with EXCLUDER Bifurcated Endoprosthesis and 26 with open surgical repair. For subjects treated with EXCLUDER Bifurcated Endoprosthesis, there were no differences between males and females for results through one year for survival, freedom from major adverse events and cumulative adverse events. For open surgical repair subjects, females compared to males as follows: results at one year showed that females had a lower rate of cumulative adverse events (0.4 vs 0.8 with p = 0.003), comparable freedom from major adverse events, and a slightly lower survival rate (87% vs 97% with p = 0.07).

10.4 Results

Tables 10.1 and 10.2 compare the subject characteristics and initial aneurysm size diameter of the EXCLUDER Bifurcated Endoprosthesis and open surgical population, respectively.

Table 10.1. Comparison of Subject Characteristics

Characteristic	EBE (N = 235)		Control (N = 99)		p-Value
	N	(%)	N	(%)	
Average Age (range in years)	73.0	(48-91)	70.1	(51-87)	0.002
Gender:					
Male	204	87%	73	74%	
Female	31	13%	26	26%	0.004
Coronary Artery Disease	145	62%	53	54%	0.165
Arrhythmia	56	24%	21	21%	0.591
Valvular Heart Disease	18	8%	7	7%	0.852
Congestive Heart Failure	22	9%	8	8%	0.708
Stroke	26	11%	10	10%	0.818
Aneurysm Symptomatic	11	5%	15	15%	<0.001
Inflammatory AAA	2	1%	1	1%	1.00
Family History of AAA	14	6%	9	9%	0.307
Other Concomitant Aneurysms	18	8%	13	13%	0.116
Peripheral Arterial Occlusive Disease	38	16%	14	14%	0.640
Prior Vascular Intervention	26	11%	10	10%	0.796
Long Term Use of Steroids	8	3%	1	1%	0.290
Thrombotic Event	17	7%	4	4%	0.332
COPD	62	26%	25	25%	0.830
Smoking History	208	89%	84	85%	0.357
Renal Dialysis	0	0	0	0	NA
Paraplegia	0	0	0	0	NA

Characteristic	EBE (N = 235) N	(%)	Control (N = 99) N	(%)	p-Value
Erectile Dysfunction (males only)	33	16%	10	14%	0.616
Hepatic Dysfunction	6	3%	1	1%	0.679
Bleeding Disorder	11	5%	1	1%	0.119
Cancer	59	25%	19	19%	0.243

Table 10.2. Aneurysm Diameter Distribution

Diameter Range	EBE (N = 235) N	(%)	Control (N = 98) N	(%)
< 30 mm	0	0%	0	0%
30-39 mm	0	0%	0	0%
40-49 mm	61	26%	15	15.3%
50-59 mm	109	46.4%	46	46.9%
60-69 mm	44	18.7%	21	21.4%
70-79 mm	15	6.4%	10	10.2%
80-89 mm	4	1.7%	5	5.1%
≥ 90 mm	2	0.9%	1	1.0%

10.4.1 Primary Outcomes: Safety and Effectiveness

Data gathered in Tables 10.3 to 10.13 were collected by either the Core Lab or the clinical study sites. Table 10.3 compares the safety and efficacy measures between the EXCLUDER Bifurcated Endoprosthesis and control subjects as reported by the clinical sites through the primary end point of 12 months.

The study design is based on one-year safety and effectiveness outcomes. Subject follow-up is continuing and two-year data are also presented.

Table 10.3. Principal Safety Results

Outcome Measures	EBE N	(%)	Control N	(%)	p-Value
Early (≤ 30-day) Mortality	3	1%	0	0	p = 0.56
Early (≤ 30-day) Adverse Events	32	14%	56	57%	p <0.0001
Early Conversion	0	0	0	0	NA
Late Conversion	0	0	0	0	NA
Rupture	0	0	0	0	NA

Three conversions have occurred >24 months postoperative due to aneurysm enlargement and/or endoleak.

Tables 10.4 to 10.11 describe results of the EXCLUDER Bifurcated Endoprosthesis subjects as reported by the Core Lab. Device performance factors analyzed by the Core Lab included device integrity (Table 10.4), device patency (Table 10.5), migration (Tables 10.6 and 10.7), and aneurysm exclusion (Tables 10.8 to 10.11). For device performance factors, more than one incident can occur to one subject and incidents are not necessarily viewed at every time point for one subject. Device integrity encompasses the structural findings of the wire-form via KUB images at the corresponding follow-up time points.

Table 10.4. Device Integrity Assessment by KUB Imaging Data

Device Integrity: KUB	Discharge (N = 171)		6 Months (N = 156)		12 Months (N = 140)		24 Months (N = 117)	
	N	%	N	%	N	%	N	%
Subjects Free From Device Integrity Issues	170	99%	156	100%	140	100%	117	100%
Fracture	1	0.6%	0	0%	0	0%	0	0%

Table 10.5. Narrowing of the Flow Channel by CT Imaging Data*

Narrowing	1 Month (N =212)		6 Months (N = 193)		12 Months (N = 185)		24 Months (N = 148)	
	N	%	N	%	N	%	N	%
EXCLUDER Bifurcated Endoprosthesis	3	1.5%	0	0%	2	1.1%	2	1.4%

*None affected device patency.

Table 10.6. CT Findings – Trunk Migration*

CT – Trunk Migration	6 Months (N = 171)		12 Months (N =175)		24 Months (N = 144)	
	N	%	N	%	N	%
Trunk Migration	5	3.0%	4	2.3%	2	1.4%

*None resulted in clinical sequelae.

Table 10.7. KUB Findings – Component Migration*

KUB – Component Migration	6 Months (N = 139)		12 Months (N = 139)		24 Months (N = 122)	
	N	%	N	%	N	%
Component Migration	2	1.4%	1	1.0%	1	1.0%

*None resulted in clinical sequelae.

Table 10.8. Endoleak Status according to Evaluation Interval

Type Endoleak[1,2]	Evaluation Interval 1-month (N = 180) N	(%)	6-months (N = 177) N	(%)	12-months (N = 156) N	(%)	24-months (N=119) N	%
Type I	7	4%	3	2%	2	1%	3	3%
Type II	21	12%	19	11%	19	12%	16	13%
Type III	0	0%	0	0%	0	0%	0	0%
Type IV	0	0%	0	0%	0	0%	0	0%
Indeterminate	11	6%	14	8%	6	4%	5	4%
Total	39	22%	36	20%	27	17%	24	20%

Table 10.9. Change in Aneurysm Size by Interval

Change in Aneurysm Size	1 month to 6 months (N = 182) N	%	1 month to 12 months (N = 181) N	%	1 month to 24 months (N = 146) N	%
Decrease	18	10%	26	14%	28	19%
No Change	159	87%	142	78%	97	67%
Increase	5	3%	13	8%	21	14%

Table 10.10. Maximum Aneurysm Diameter and Endoleaks at 12-Months

Aneurysm Change from 1 to 12 Months*	N	Endoleak at 12 Months* N	%	p-Value
Increase (≥ 5 mm)	10	4	40%	
No Change	118	19	16%	
Decrease (≤ 5 mm)	18	2	11%	
Total	146	25	17%	0.12

*Only includes patients with interpretable films (endoleak) and measurements of aneurysm change from 1 to 12 months.

Table 10.11. Maximum Aneurysm Diameter and Endoleaks at 24-Months

1-month to 24-month Aneurysm Change*	N	Endoleak at 24-months* N	%	p-Value
Increase (≥5 mm)	15	7	47%	
No change	74	10	14%	
Decrease (≤5 mm)	23	2	9%	
Total	112	19	17%	0.004

*includes subjects with interpretable films for endoleaks and measurements for aneurysm change from 1 to 24 months.

Secondary interventions within the first and second year each were performed in 6% of the EXCLUDER Bifurcated Endoprosthesis subjects as shown in Table 10.11. All interventions were catheter-based. Subjects may have a single intervention for an endoleak and an aneurysm enlargement.

Table 10.12. Interventions for Endoleak and Aneurysm Size Increases

Intervention	Post-procedure to 12-months (N = 235) N	(%)	> 12-months to 24-months (N = 203) N	(%)
Number subjects with ≥ 1 Intervention	15	6%	12	6%
Treatment of Endoleaks:	16	7%	10	5%
Embolization	15		9	
Ligation	1		0	
Conversion	0		1*	
Treatment of Aneurysm Enlargement	1	0.4%	8**	4%
Embolization	0		5	
Ligation	1		0	
Conversion	0		3*	

*Total of three conversions
**Six of the subjects also had endoleak.

10.4.2 Secondary Outcomes

As described in Table 10.13, treatment of AAA with EXCLUDER Bifurcated Endoprosthesis compared to the control group demonstrated significant benefits in recovery and quality of life measures.

Table 10.13. Secondary Outcomes by Treatment Group

Secondary Outcomes	EBE	Control	p-Value
Blood Loss (ml) Mean (range)	310 (50-2160)	1590 (100-7000)	<0.0001
Procedure Transfusion (%)	14%	89%	<0.0001
Procedure Time (minutes) Mean (range)	144 (51-320)	196 (67-420)	<0.0001
ICU Stay (%)	24%	87%	<0.0001
Hospital Length of Stay (days) Mean (range)	2 (1-11)	9.8 (3-114)	<0.0001
Time to First Oral Intake (days) Mean (range)	0.5 (0.-2.1)	2.6 (0.07-9.5)	<0.0001
Time to Ambulation (days) Mean (range)	1.0 (0-5.0)	2.6 (0-18)	<0.0001
Time to Return to Normal Activities (Days)	42	92	0.002

11.0 Conclusions Drawn from the Studies

As compared to conventional open surgery, the clinical benefits of the EXCLUDER Bifurcated Endoprosthesis are a lower rate of major complications, reduced blood loss and blood replacement volume, reduced need for an ICU stay, shorter hospitalization and faster return to normal activities. The risks include procedure- and/or device-related phenomenon, which include but are not limited to endoleaks and increase in aneurysm size.

[1] White GH, May J, Waugh RC, et al. Type II and Type IV endoleak: Toward a complete definition of blood flow in the sac after AAA endoluminal repair. J Endovasc Surg 5:305-309, 1998.

[2] White GH, Yu W, May J, et al. Endoleak as a complication of endoluminal grafting of abdominal aortic aneurysms: Classification, incidence, diagnosis and management. J Endovasc Surg 4:152-168, 1997.